IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA

ASTRAZENECA AB and
ASTRAZENECA PHARMACEUTICALS LP,

Plaintiffs,

v. **CIVIL ACTION NO. 1:18CV193**
(Judge Keeley)

MYLAN PHARMACEUTICALS INC. and
KINDEVA DRUG DELIVERY L.P.,

Defendants.

c/w 1:19CV203

MEMORANDUM OPINION AND ORDER MAKING FINDINGS OF FACT AND GRANTING JUDGMENT IN FAVOR OF THE PLAINTIFFS, ASTRAZENECA AB AND ASTRAZENECA PHARMACEUTICALS LP

I. BACKGROUND

In this patent infringement action, the plaintiffs, AstraZeneca AB and AstraZeneca Pharmaceuticals LP (collectively, "AstraZeneca"), and the defendants, Mylan Pharmaceuticals Inc. and Kindeva Drug Delivery L.P.[1] (collectively, "Mylan"), dispute whether claims 9, 10, 13, and 14 of United States Patent No. 7,759,328 ("the '328 Patent"); claims 12, 13, 18, and 19 of United States Patent No. 8,143,239 ("the '239 Patent"); and claims 10 and 19 of United States Patent No. 8,575,137 ("the '137 Patent") (collectively, "the asserted claims" or the "patents-in-suit") are

[1] Although AstraZeneca originally included 3M Company as a defendant in this action, the parties stipulated to its dismissal because all activities related to the generic Symbicort® program under review by the FDA as ANDA No. 211699 were transferred from 3M to Kindeva (Dkt. No. 386).

valid and enforceable (Dkt. Nos. 285 at 4, 5; 286 at 4, 5; 390).[2] The asserted claims are associated with Symbicort®, AstraZeneca's New Drug Application ("NDA") product approved by the FDA as a treatment for asthma in patients six years of age and older, and as a maintenance treatment in patients with chronic obstructive pulmonary disease (Dkt. Nos. 285 at 3, 4; 286 at 3, 4). Mylan has filed an Abbreviated New Drug Application ("ANDA") seeking to engage in the commercial manufacture, use, or sale of generic versions of the two dosage forms of Symbicort®, prior to the expiration of the patents-in-suit.

The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, otherwise known as the "Hatch-Waxman Act", seeks to encourage "pioneering research and development of new drugs," as well as the "production of low-cost, generic copies of those drugs." Eli Lilly & Co. v. Teva. Pharm. USA, Inc., 557 F.3d 1346, 1348 (Fed. Cir. 2009). To that end, a manufacturer may obtain Food and Drug Administration ("FDA") approval to market a generic drug by making a certification that each patent listed in the FDA's Approved Drug Products with

[2] All docket and page numbers refer to the numbers assigned by the Court's electronic docket. Unless indicated otherwise, all docket numbers refer to Case No. 1:18CV193.

Therapeutic Equivalence Evaluations ("the Orange Book") as covering the NDA drug are "invalid or will not be infringed by the manufacture, use, or sale of the new generic drug for which the ANDA is submitted" ("paragraph IV certification"). Id. (citing 21 U.S.C. § 355(j)(2)(A)(vii)(IV)). Upon receiving a paragraph IV certification, a patentee may sue the applicant for patent infringement within 45 days, thus delaying FDA approval of the ANDA. Id. (citing 21 U.S.C. § 355(j)(5)(B)(iii)).

In this case, in which AstraZeneca has sued Mylan under the Hatch-Waxman Act for infringement of the patents-in-suit, the Court is tasked with deciding whether the asserted claims of AstraZeneca's patents are invalid as obvious under 35 U.S.C. § 113.[3] As discussed below, the Court **CONCLUDES** that

[3] Initially, four patents associated with Symbicort® were at issue in this case. These include U.S. Patent Nos. 7,759,328; 8,143,239; 8,575,137; and 7,967,011 (the "'011 patent) (Dkt. No. 1; Case No. 1:19CV203, Dkt. No. 1). On November 12, 2019, AstraZeneca amended its complaint to add infringement claims for U.S. Patent No. 10,166,247 (the "'247 patent") (Dkt. No. 89), and deleted its previous claims related to the '011 Patent from the amended complaint.

Thereafter, on September 21, 2020, the parties stipulated to the dismissal of all claims, counterclaims, and defenses regarding the '247 patent (Dkt. No. 349). Mylan also stipulated that their generic product infringed the ten asserted claims at issue and that AstraZeneca's product, Symbicort®, embodied the claims. Id.

Mylan has failed to demonstrate by clear and convincing evidence that the asserted claims of the patents-in-suit are invalid for obviousness.

II. FINDINGS OF FACT

A. The Parties, Jurisdiction, and Venue

AstraZeneca AB is a corporation organized under the laws of Sweden, with its principal place of business at S-151 85 Södertälje, Sweden. AstraZeneca Pharmaceuticals LP is a limited partnership organized under the laws of the State of Delaware, with its principal place of business at 1800 Concord Pike, Wilmington, Delaware 19803. Mylan Pharmaceuticals Inc. is a company organized under the laws of the State of West Virginia with its principal place of business at 781 Chestnut Ridge Road, Morgantown, West Virginia 26505. Kindeva Drug Delivery L.P. is a company organized under the laws of the State of Delaware, with a place of business at 42 Water Street, Building 75, St. Paul, Minnesota 55170. The Court has subject matter and personal jurisdiction, and venue is proper.

Thus, based on the parties' various stipulations, the only remaining issue at trial was whether the asserted claims are invalid as obvious under § 113.

B. Factual and Procedural Background

Because the asserted claims of the patents-in-suit recite a specific method for treating asthma and COPD, the Court begins its analysis with a brief discussion of these respiratory disorders, as well as a review of the development of the Symbicort® pMDI and the relevant prosecution history of AstraZeneca's patent applications related to Symbicort®.

1. Asthma and COPD

a. Asthma

Asthma "is a reversible inflammatory condition of the lungs." (Trial Trans. 356:12-14). The reversibility of asthma is important as compared to other respiratory conditions, like COPD, where the changes may be fixed. Id. at 356:14-16. Any inflammation in the lungs can interfere with the exchange of carbon dioxide for oxygen. Id. at 356:17-21. This interference can lead to hypoxia (oxygen starvation), and death if not addressed. Id. at 356:19-23. An individual suffering an asthma attack will cough, wheeze, and experience shortness of breath. Id. at 356:14-25, 357:1-2. Medications that control asthma symptoms target the actual site of the inflammation. Id. at 357:3-11.

Of chief concern in an asthma attack is the airway obstruction

caused by this inflammation, which may be triggered by the patient's environment, allergies, or acute illness. Id. at 357:18-358:1. Mylan's expert, Dr. Ulus Atasoy, analogized escalating lung inflammation in an asthma attack to a small snowball rolling down a hill, growing in intensity before potentially leading to severe asthma attack or death. Id. at 358:1-3. According to Dr. Atasoy, targeting this inflammation in the lungs results in a better chance of controlling the attack. Id. at 358:4-8. Inhaled corticosteroids ("ICS") are used to reduce the inflammation in the lungs and the swelling and tightening of the airways. Id. at 358:9-11. Long-acting beta agonists ("LABAs") are used to open the airways. Id. at 358:11-13.

b. COPD

Unlike asthma, chronic obstructive pulmonary disease ("COPD") is a fixed inflammatory condition of the lungs (Trial Trans. 356:13-16). Except for Symbicort®, no other ICS LABA pMDIs indicated for COPD are available in the United States. Id. at 836:5-7.

2. Development of Symbicort®

a. Montreal Protocol

The first pressurized metered dose inhalers launched in the

1950s used chlorofluorocarbon ("CFC")-based propellants (Dkt. No. 415 at 10). In 1989, however, the Montreal Protocol recognized CFCs as harmful to the environment. As a consequence, these types of propellants were phased out of production (DTX 1017, JTX 2403).

In connection with that phase out, two consortia from several pharmaceutical companies were formed to generate safety data on the two hydrofluoroalkane ("HFA") propellants identified as suitable for product use: HFA 134a and HFA 227 (JTX 2403.0048-49). The International Pharmaceutical Aerosols Consortium for Toxicology I ("IPACT I") was formed in August 1990 to examine HFA 134a. Id.; see also DTX 1017.60. The International Pharmaceutical Aerosols Consortium for Toxicology II ("IPACT II") was formed in February 1991 to study HFA 227. Id. As a result of those studies, in July 1994, regulatory authorities approved the IPACT I toxicology data for HFA 134a as suitable for pMDI use. Later, in September 1995, the IPACT II data for HFA 227 was approved. Id.

b. Delivery of Respiratory Drugs

Several delivery systems are available to administer inhaled medications. These include nebulizers, dry powder inhalers ("DPI"), and pressurized metered dose inhalers ("pMDI"). Each of these systems has a different method for transporting inhalable

medications into a patient's lungs.

Nebulizers use pressurized air with a solution to breathe the medication into the lungs (Trial Trans. 359:8-11). Nebulizers are not portable and require regular cleaning. Id. at 105:18-20. Before the advent of metered dose inhalers and DPIs, these respiration treatments were the only maintenance treatment available, and they proved challenging for young asthmatics. Id. at 359:14-18. Nebulizers are now typically used only in hospital settings to administer emergency treatments for asthma attacks. Id. at 359:11-13.

DPIs are breath-actuated and introduce a specific amount of dry powder formulation into a patient's lungs. Id. at 360:5-9. In order to use DPIs, the patient must take a deep, fast breath. Id. at 360:10-11. But individuals experiencing a respiratory attack may not be able to produce such a breath. Id. at 360:11-13. Further, because treatment with a DPI depends on the respiratory force a patient generates, use of this kind of inhaler is challenging for young children, elderly individuals, and those with neurological impairments. Id. at 101:10-12; 360:13-16. If the patient cannot generate an adequate breath, the medicine will not be delivered to the lower airways. Id. at 832:8-11.

PMDIs contain gas which is liquified under pressure. Id. at 106:21-22. Mylan's formulation expert, Dr. John Pritchard, testified that using a pMDI is like operating a consumer aerosol; the patient presses a button on the can, "and the spray comes out." Id. at 106:22-24. In contrast to a consumer aerosol, however, pMDIs have a metering valve, which controls the dose the patient receives. Id. at 106:25, 107:1-5.

According to Dr. Pritchard, newly diagnosed asthma patients are given Albuterol, a rescue medication,[4] in a pMDI format. Id. at 107:6-10. This is because the pMDI does not require a deep breath for an adequate dose. Id. at 107:8-11. The liquified gas held under pressure does all the work needed to get the medication into the patient's lungs. Id. Dr. Pritchard believes that providing all newly diagnosed patients with an Albuterol pMDI rescue inhaler means that patients are familiar with these types of devices and need not learn how to use DPIs. Id. at 107:11-13.

When patients use pMDIs, the inhaler is typically shaken

[4] A rescue medication is different from a controller, or maintenance, therapy (Trial Trans. 830:13-15). A controller therapy is taken every day to manage a patient's symptoms. Id. Symbicort® maintains its effect for twenty-four (24) hours when used twice per day. Id. at 834:22-25.

before being placed into the mouth and actuated. Id. at 832:14-16. According to Dr. Reynold Panettieri, AstraZeneca's expert clinician, it typically takes a patient about twenty seconds to actuate a pMDI after shaking it. Id. at 832:19-21. The optimal use of the inhaler also depends on a patient's ability to coordinate actuating the inhaler and taking a breath. Id. at 832:22-833:3. Patients who are very young, very old, or cognitively impaired may experience some delay between shaking the inhaler and taking a breath. Id. Dr. Panettieri testified that it is critically important to the effective treatment of patients with asthma and COPD to deliver a consistent and reproducible dose of an inhaled drug into the patient's lower airways. Id. at 833:10-17.

3. Prior Art

a. Mistry

Mistry is the lead inventor on related foreign and United States patents and patent applications titled "Pressurized aerosol compositions" and directed primarily to polymers that work in HFA propellants to stabilize pMDI suspension formulations. (JTX 2381.0001-2).

The invention claimed in Mistry is:

a pressurized aerosol composition . . . that comprises a

> liquefied hydrofluoroalkane, a medicinal product in powder form dispersible therein and a polymer soluble in the liquefied hydrofluoroalkane, wherein the polymer includes repeating structural unites, the units being selected from units that contain an amide and units that contain an ester of a carboxylic acid.

Id. at pp. 2-3.

Relevant to the patents-in-suit, Mistry disclosed polymers soluble in HFA propellants. Id. at p. 2 ("We have now found, surprisingly, that certain polymers are both soluble in aerosol propellants and are able to stabilize pharmaceutical compositions."). Mistry also disclosed preferred hydrofluoroalkanes of HFA 134a, HFA152a, and HFA 227. Id. at p. 5. Of these, compositions including HFA 227 were particularly preferred. Id.

Mistry particularly preferred a polymer containing 1-ethylene-pyrrolidin-2-one, i.e., polyvinylpyrrolidone ("PVP"). Id. at p. 3. Mistry found that a "wide variety of molecular weights" provided acceptable suspensions. Id. PVP is usually characterized by its K value, "where K is determined from measurements of viscosity using the Fikentscher equation." Id. Mistry particularly preferred polymers with K values from 10 to 150, with a specific preference for 15 to 120. Id. "The particular K values and ranges that may be mentioned include 10-14, 15-18, 29-32, 88-100 and 115-125." Id.

Mistry also disclosed polymers containing a carboxylic acid ester and repeating structural units such as polyvinyl acetate and copolymers of vinyl acetate and vinylpyrrolidone. Id. at pp. 3-4. It also included acrylic acid/methacrylate copolymers. Id. at p. 4. "The amount of polymer in the composition will depend on the active ingredient that is to be dispersed, its concentration and the particular polymer selected; however, in general the amount of polymer is from 0.00001 to 10% w/w, preferably 0.0001 to 5% w/w and especially 0.001 to 1% w/w." Id.

Lubricants disclosed by Mistry include polyethoxylated compounds, "especially polyethylene glycol with an average molecular weight from 200 to 3000," with 400 to 2000 being preferred. Id. Mistry also disclosed polysorbates, alkyl aryl polyether alcohols, and lubricating excipients like fully halogenated chlorofluorocarbons of high molecular weight and medium-chain fatty acids. Id. A concentration from 0.01 to 4% w/w was preferred, with the most preferable being between 0.1 to 2% w/w. Id. at 4-5.

Mistry contemplated numerous medicaments that may be dispersed in a propellant mixture, including drugs such as sodium cromoglycate, nedocromil sodium, inhaled steroids like budesonide,

bronchodilators like salbutamol, reproterol, and formoterol, anticholinergics, and combinations of two or more agents. Id. at 6. Mistry listed sodium cromoglycate and salbutamol as an example of a combination of two agents. Id.

b. Rogueda

Rogueda disclosed a number of medicines, excipients, and lubricants that could be included in pMDIs (JTX-2001.0170). Particularly relevant to the claims in this case, Rogueda used a series of control samples to compare directly to novel formulations. Id. at p. 180. Two of these samples included ingredients relevant to the claims at issue:

- Control 3: Formoterol Fumarate Dihydrate with PEG 1000 and PVP K25 in a HFA 227 and 134a mix.
- Control 9: Budesonide with PEG 1000 and PVP K25 in HFA 227.

Id. at p. 189.

Control 3 included the following concentrations of ingredients:

Formoterol Fumarate Dihydrate: 0.0167% w/w
PEG 1000: 0.1% w/w
PVP K25: 0.001% w/w
HFA 227: 25% w/w
HFA 134a: to 100% w/w

Id. at p. 195. Control 9 included the following concentrations of ingredients:

Budesonide: 0.259% w/w
PEG 1000: 0.3% w/w
PVP K25: 0.001% w/w
HFA 227: to 100% w/w

Id.

Rogueda found that samples prepared with HFA 134a were on average better than the ones prepared with HFA 227 due, primarily, to the differences in the chemicals' densities. Id. at 197. The budesonide examples, when compared with controls 7, 8, and 9, demonstrated a drastic reduction in the amount of drug adhesion to the wall of the can. Id. The formoterol fumarate dihydrate examples 3, 4, 8, and 11, when compared with controls 1, 2, and 3, showed similar drastic improvement over respective control samples. Id.

c. Intal and Tilade

Intal and Tilade are mast cell stabilizer pMDI products intended to treat asthma and were approved by regulatory authorities[5] prior to the priority date (Dkt. No. 415 at 10, Trial

[5] Although marketed and sold in markets outside of the United States, Intal and Tilade were not approved by the FDA at the priority date (Trial Trans. at 700:4-7).

Trans. at 700:13-14). Each product contains PVP, PEG, and an active ingredient suspended in propellant HFA 227. JTX 2376, JTX 2383. However, both Intal and Tilade use different grades of PVP and PEG from those used in the Symbicort® pMDI formulation (Dkt. No. 415 at 11, 12). Additionally, both products use significantly higher doses of their active ingredients than those used in the claimed formulation (Trial Trans. at 700:14-18).

4. Brief Summary of Prosecution History of Patents-In-Suit

The Patent and Trademark Office ("PTO") issued the patents-in-suit after considering, inter alia, Mistry and Rogueda and concluding that the claims were not obvious (JTX 2023.0002, 2001.0825, JTX2003.0328, JTX2005.0333). The PTO, however, rejected claims 1-12 of the '328 patent as unpatentable over Meade et al and Weers et al. (JTX 2001.0327). "Meade teaches that the formoterol can exist in the form of formoterol fumarate . . . [and] that propellant gas such as HFA-227, co-solvent such as polyethylene glycol (PEG), and surfactants such as polyvinylpyrrolidone (PVP) can be added [to] the composition." Id. The PTO also noted that Meade did not teach "(1) an exemplified pharmaceutical composition comprising budesonide, formoterol, HFA227, PEG, and PVP[,] and administering the composition to a patient having a respiratory

disorder; (2) the instant types of PEG such as PEG 1000 and PVP such as PVP K25; [and] (3) the instant amounts of PVP and PEG." Id.

Weers taught that drugs such as budesonide and formoterol were administered to patients to treat respiratory disorders. Id. at pp. 327-28. According to the PTO, it would have been obvious to "one having ordinary skill in the art to have modified the invention of Meade to additionally administer the pharmaceutical composition to a patient for the treatment of respiratory disease." Id. at p. 328.

The patent applicants, Drs. Nayna Govind and Maria Marlow (the "Applicants"), contended before the PTO that the claims were not obvious in light of the teachings of Meade and Weers. Id. at p. 344. They stressed that neither Meade nor Weers disclosed a pharmaceutical composition containing PVP at a concentration of 0.001% w/w, id., stating they had "in fact made the surprising discovery that 0.001% w/w PVP gave 'consistently stable formulations over the required dose range, incorporating a wide range of concentrations of the active components, and at a much lower concentration than indicated in the prior art.'" Id. at p. 345 (quoting Specification at page 2).

The PTO ultimately rejected claims 1-3, 5-9, and 12 as obvious over Meade. Id. at p. 429. Claims 13 to 15 were added to this

rejection, and the Examiner concluded that the Applicants had not shown the criticality of the invention comprising 0.001% w/w PVP. Id. at p. 430.

On July 27, 2007, the Applicants appealed to the Board of Patent Appeals and Inferences from the final rejection of claims 1-3, 5-9, and 12-15. Id. at p. 434. After additional amendments and rejections, the Board Examiner allowed the claims because the "results provided in the specification on pages 7-9 for the stability of the instant composition overcomes any obviousness type rejection. . . . The claimed invention is specific to chemical components and amounts thereof." Id. at p. 602.

5. Inter Partes Review

On July 24, 2017, the PTO adjudicated a petition for inter partes review of claims 1-15 of the '328 patent. Id. at p. 888. Pursuant to the "reasonable likelihood" standard of 35 U.S.C. § 314(a), the Patent Trial and Appeal Board ("PTAB") concluded that the petitioner had not established a reasonable likelihood that it would prevail in showing the unpatentability of "claims 1 and 4-15 over the combined teachings of Mistry, Rogueda, and Carling because each of those claims requires a pharmaceutical composition comprising formoterol fumarate dihydrate at a concentration of 0.09

mg/ml in combination with specific values and concentrations and/or weight percentages of budesonide, PVP K25, and PEG 1000." Id. at pp. 907-908.

6. The Asserted Claims

a. The '328 Patent

The '328 Patent, filed on January 29, 2003, is titled "Composition for Inhalation," and lists Drs. Govind and Marlow as inventors (JTX 2023). The patent lists AstraZeneca AB as the assignee. The relevant claims of the patent are as follows:

1. A pharmaceutical composition comprising formoterol fumarate dihydrate, budesonide, 1,1,1,2,3,3,3-heptafluoropropane (HFA 227), PVP K25 (polyvinyl pyrrolidone with a nominal K-value of 25), and PEG-1000 (polyethylene glycol with an average molecular weight of 1,000), wherein the formoterol fumarate dihydrate is present at a concentration of 0.009 mg/ml, the budesonide is present at a concentration in the range of 1 mg/ml to 8 mg/ml, the PVP K25 is present at a concentration of 0.001% w/w, and the PEG-1000 is present at a concentration of 0.3% w/w.

...

4. A method of treating symptoms of a respiratory disorder, comprising administering to a patient the pharmaceutical

composition according to claim **1**, wherein the respiratory disorder is asthma, rhinitis, or chronic obstructive pulmonary disease (COPD).

...

9. The method of claim **4**, wherein the concentration of budesonide is 2 mg/ml.

10. The method of claim **4**, wherein the concentration of budesonide is 4 mg/ml.

...

13. A pharmaceutical composition comprising formoterol fumarate dihydrate, budesonide, HFA 227, PVP K25, and PEG-1000, wherein the formoterol fumarate dihydrate is present at a concentration of 0.09 mg/ml, the budesonide is present at a concentration of 2 mg/ml, the PVP K25 is present at a concentration of 0.001% w/w, and the PEG-1000 is present at a concentration of 0.3% w/w.

14. A pharmaceutical composition comprising formoterol fumarate dihydrate, budesonide, HFA227, PVP K25, and PEG-1000, wherein the formoterol fumarate dihydrate is present at a concentration of 0.09 mg/ml, the budesonide is present at a concentration of 4 mg/ml, the PVP K25 is present at a concentration

of 0.001% w/w, and the PEG-1000 is present at a concentration of 0.3% w/w.

AstraZeneca has alleged that Mylan's ANDA product will infringe claims 9, 10, 13, and 14.

b. The '239 Patent

The '239 Patent, filed on May 28, 2010, is titled "Composition for Inhalation," and lists Drs. Govind and Marlow as inventors (JTX 2024). The patent lists AstraZeneca AB as the assignee. The relevant claims of the patent are as follows:

10. A pressurized metered dose inhaler containing a suspension composition comprising formoterol fumarate dihydrate in the form of particles; budesonide in the form of particles; 1,1,1,2,3,3,3-heptafluoropropane (HFA 227); PVP K25 (polyvinyl pyrrolidone with a nominal K-value of 25); and PEG-1000 (polyethylene glycol with an average molecular weight of 1,000); wherein the budesonide is present at a concentration in the range of 1 mg/ml to 8 mg/ml; the PVP K25 is present at a concentration of 0.001% w/w; and the PEG-1000 is present at a concentration of 0.3% w/w, and wherein an actuation of the inhaler delivers 4.5 µg formoterol fumarate dihydrate and 40 to 320 µg budesonide.

...

12. The inhaler of claim **10**, wherein an actuation of the inhaler delivers 80 µg budesonide.

13. The inhaler of claim **10**, wherein an actuation of the inhaler delivers 160 µg budesonide.

...

16. A method of administering an inhalable composition to a patient, the method comprising

> providing a pressurized metered dose inhaler containing a suspension composition comprising formoterol fumarate dihydrate in the form of particles, budesonide in the form of particles, HFA 227, PVP K25, and PEG-1000, wherein the budesonide is present at a concentration in the range of 1 mg/ml to 8 mg/ml; the PVP K25 is present at a concentration of 0.001% w/w; and the PEG-1000 is present at a concentration of 0.3% w/w, and wherein an actuation of the inhaler delivers 4.5 µg formoterol fumarate dihydrate and 40 to 320 µg budesonide; and

causing the patient to inhale the composition from the inhaler.

...

18. The method of claim **16**, wherein an actuation of the inhaler delivers 80 µg budesonide.

19. The method of claim **16**, wherein an actuation of the inhaler delivers 160 µg budesonide.

AstraZeneca has alleged that Mylan's ANDA product will infringe claims 12, 13, 18, and 19.

c. The '137 Patent

The '137 Patent, filed on March 5, 2012, is titled "Composition for Inhalation," and lists Drs. Govind and Marlow as inventors (JTX 2021). The patent lists AstraZeneca AB as the assignee. The relevant claims of the patent are as follows:

9. A pharmaceutical suspension composition comprising formoterol fumarate dihydrate, budesonide, HFA 227, PVP K25, and PEG-1000, wherein the budesonide is present at a concentration in the range of 1 mg/ml to 8 mg/ml and the PVP K24 is present at a concentration of 0.001 w/w.

10. The pharmaceutical suspension composition of claim **9**, wherein the PEG-1000 is present at a concentration of 0.3% w/w.

...

19. A method of treating a respiratory disorder, the method comprising administering the pharmaceutical suspension composition of claim **10** to a patient identified as in need of treatment with the composition.

AstraZeneca has alleged that Mylan's ANDA product will infringe claims 10 and 19.

7. Claim Construction

On August 12, 2020, the Court construed the claim term "0.001%," which appears in several claims in the patents-in-suit, to have its ordinary and plain meaning (Dkt. No. 317). AstraZeneca argued that "0.001%" should be construed to have its plain meaning, which is "0.001%, expressed using one significant digit." (Dkt. No. 292 at 5). Mylan contended that "0.001%" meant "that precise number, with only minor variations" because AstraZeneca abandoned its proposed construction of "0.001%" during prosecution of the patents-in-suit (Dkt. No. 288 at 4). After reviewing the claim language, the patent specifications, and the prosecution history, the Court determined that AstraZeneca's proposed construction was consistent with the claim language and specification of the patents-in-suit.

Additionally, while the parties were briefing competing interpretations of the term "pharmaceutical composition," AstraZeneca agreed to adopt Mylan's proposed construction of a "suspension for therapeutic administration," rather than "a suspension that is suitable for therapeutic administration." (Dkt. No. 320).

III. CONCLUSIONS OF LAW

A. Applicable Legal Standards

1. Burden of Proof

Each of the asserted claims is presumed to be valid. See 35 U.S.C. § 282; Microsoft Corp. v. I4i Ltd. P'ship, 564 U.S. 91, 94, 131 S.Ct. 2238, 2243 (2011); Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd., 719 F.3d 1346, 1352 (Fed. Cir. 2013). Mylan thus bears the burden of proving invalidity by clear and convincing evidence. See 35 U.S.C. § 282 ("The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity."); Microsoft Corp., 564 U.S. at 102, 131 S.Ct. at 2246 ("[A] defendant raising an invalidity defense [bears] a heavy burden of persuasion, requiring proof of the defense by clear and convincing evidence." (citation omitted) (internal quotation marks omitted)). "Clear and convincing evidence places in the fact finder 'an abiding conviction that the truth of [the] factual contentions are highly probable.'" Procter & Gamble Co. v. Teva Pharm. USA, Inc., 566 F.3d 989, 994 (Fed. Cir. 2009) (quoting Colorado v. New Mexico, 467 U.S. 310, 316, 104 S.Ct. 2433 (1984)).

"The burden of proof never shifts to the patentee to prove validity." Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1359 (Fed.

Cir. 2007). But, when determining whether Mylan has met its burden of proof, the Court must consider all of the evidence presented at trial, including the testimony and evidence offered by AstraZeneca. See id. at 1360.

2. Obviousness

A patent will not issue or may be invalidated if the subject matter of the patent is obvious.

> A patent may not be obtained . . . if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

35 U.S.C. § 103 (hereafter, "Section 103"). Obviousness is a question of law, which depends on several underlying factual inquiries. Richardson-Vicks Inc. v. Upjohn Co., 122 F.3d 1476, 1479 (Fed. Cir. 1997).

> Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc. might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406, 127 S.Ct. 1727

(2007) (quoting Graham v. John Deere Co., 383 U.S. 1, 17-18, 86 S. Ct. 684 (1966)). "[W]hile an analysis of any teaching, suggestion, or motivation to combine known elements is useful to an obviousness analysis, the overall obviousness inquiry must be expansive and flexible." In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation, 676 F.3d 1063, 1069 (Fed. Cir. 2012) (citing KSR, 550 U.S. at 415, 419, 127 S.Ct. 1727).

"To render a claim obvious, prior art cannot be 'vague' and must collectively, although not explicitly, guide an artisan of ordinary skill toward a particular solution." Unigene Labs., Inc. v. Apotex, Inc., 655 F.3d 1352, 1361 (Fed. Cir. 2011) (citing Bayer Schering Pharm. AG v. Barr Labs., Inc., 575 F.3d 1341, 1347 (Fed. Cir. 2009)). "[M]ost inventions that are obvious were also obvious to try," and a "combination is only obvious to try if a person of ordinary skill has a 'good reason to pursue the known options.'" Unigene, citing KSR, 550 U.S. at 421. "When a field is unreduced by direction of the prior art,' and when prior art gives 'no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful, an invention is not obvious to try.'" Unigene, quoting Bayer Schering, 575 F.3d at 1347 (additional citations omitted).

B. Defining the Level of Ordinary Skill in the Art

Determining who constitutes a person of ordinary skill in the art ("POSA") is a factual question involving a two-step inquiry to determine (1) what exactly is that "relevant art" at issue, and (2) who qualifies as a "person of ordinary skill" in that art. Seed Research Equip. Solutions, LLC v. Gary W. Clem, Inc., No. 09-01282-EFM-KGG 2011 WL 5024351, at *3 (D. Kan. Oct. 20, 2011) (citing Arachnid, Inc. v. Merit Indus., Inc., 201 F. Supp. 2d 833, 888 (N.D. Ill. 2002).

Regarding patents, "art" is defined as "[a] field of useful endeavor." Art, Black's Law Dictionary (11th ed. 2019) And "relevant art" is the "[a]rt to which one can reasonably be expected to look for a solution to the problem that a patented device tries to solve." Id. "The relevant art is defined by the nature of the problem confronting the would-be inventor." Ryko Mfg. Co. v. Nu-Star, Inc., 950 F.2d 714, 716 (Fed. Cir. 1991) (internal quotation omitted). "Factors that may be considered in determining level of ordinary skill in the art include: (1) the educational level of the inventor; (2) types of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology;

and (6) educational level of active workers in the field." Daiichi Sankyo Co., Ltd. v. Apotex, Inc., 501 F.3d 1254, 1256 (Fed. Cir. 2007) (citation omitted). These factors are illustrative, not exhaustive. Id.

In this case, the parties agree that, for the formulation claim, a POSA at the priority date would have been a person with at least (1) an advanced degree, such as a master's degree or Ph.D., in a pharmaceutical science, such as a formulation science; (2) several years of experience in the field of aerosol pharmaceutical development; and (3) the ability to collaborate with others, such as colleagues with expertise in related areas (i.e., physicians specializing in treating respiratory diseases) (Dkt. No. 415 at 7). AstraZeneca asserts that a POSA would also be trained in chemistry (Dkt. No. 417 at 7). Mylan's expert, Dr. Pritchard, explained that a POSA would be able to consult with colleagues having expertise in chemistry if and when necessary (Trial Trans. 95:15-24, 154:4-20; 156:18-157:6; see also id. at 340:15-341:16).

The parties also offered slightly different definitions of the level of ordinary skill in the art required for the method of treatment claim. According to Dr. Atasoy, a POSA for the method of treatment would have a medical degree and at least several years of

experience with patients, such as those with asthma and COPD. Id. at 361:12-20. A POSA may collaborate with other colleagues, including experts in the field of aerosol pharmaceutical developments. Id. at 361:20-22. According to Dr. Panettieri, a POSA would have a medical degree with several years of experience in treating respiratory diseases such as COPD and asthma, id. at 837:11-13, and may collaborate with others, including a scientist with experience in the development of inhaled pharmaceutical products. Id. at 837:14-16.

These slight differences in the parties' proposed definitions would not impact the opinion of either the formulator or method of treatment expert. Id. at 118:1-18, 362:1-4, 599:4-18, and 837:20-22. Therefore, the Court determines that a formulator POSA would have an advanced degree such as a master's degree or Ph.D. in a pharmaceutical science, several years of experience in the field of aerosol pharmaceutical development, and the ability to collaborate with others, including experts in the field of chemistry or chemical engineering. A method of treatment POSA would have a medical degree and at least several years of experience treating patients with respiratory problems, such as asthma or COPD, and may collaborate with other colleagues, including expert formulators in

the field of aerosol pharmaceutical products.

C. The Parties' Contentions

Mylan contends that the patents-in-suit are invalid as obvious because the claimed formulations would have been an obvious pMDI reformulation of the Symbicort® Turbuhaler DPI ("Symbicort® DPI"). According to Mylan, a POSA would have been motivated to reformulate the Symbicort® DPI as a pMDI while maintaining its proven dosing and efficacy. Further, with only two pMDI formats available, a suspension would have been both obvious and preferred. HFA 227 would have been the preferred non-CFC propellant of the two readily available options, and a POSA would have selected PVP and PEG as excipients based on the prior art. Finally, a POSA would have optimized excipient grades and concentrations through routine testing with a reasonable expectation of success.

AstraZeneca asserts that Mylan has not met its burden to prove obviousness by clear and convincing evidence. It argues that the prior art on which Mylan relies teaches away and would not have motivated a POSA to make the claimed combination. It also contends that Mylan failed to show it would have been obvious to select and combine the elements of the claimed invention because a POSA would not have been motivated to make a suspension, to use HFA 227, PVP

K25, or PEG-1000, and would not have arrived at the claimed formulation by routine optimization or otherwise. AstraZeneca further argues that a POSA would not have had a reasonable expectation of success, and that the claimed invention exhibits unexpected properties.

The Court will address each of the parties' arguments in turn.

D. The Asserted Claims are Valid and Not Obvious

The patents-in-suit claim a new formulation to deliver budesonide and formoterol fumarate dihydrate. Therefore, the claimed invention is obvious if a person of ordinary skill would have selected and combined the prior art references to reach the claimed composition or formula. Eli Lilly and Co. v. Zenith Goldline Pharm., 471 F.3d 1369, 1380 (Fed. Cir. 2006) ("[T]o establish a prima facie case of obviousness based on a combination of elements in the prior art, the law requires a motivation to select the references and to combine them in the particular claimed manner to reach the claimed invention.").

1. Motivation to Select

As the party bearing the burden of proof, Mylan must show a "reason that would have prompted [a POSA] to combine the elements in the way the claimed new invention does," with a reasonable

expectation of success in solving a known problem. KSR, 550 U.S. at 418; Orexo AB v. Actavis Elizabeth LLC, 903 F.3d 1265, 1271 (Fed. Cir. 2018). "The obviousness inquiry does not merely ask whether a skilled artisan could combine the references, but instead asks whether 'they would have been motivated to do so.'" Adidas AG v. Nike, Inc., 963 F.3d 1355, 1359 (Fed. Cir. 2020) (quoting InTouch Techs., Inc. v. VGO Commc'ns, Inc., 751 F.3d 1327, 1352 (Fed. Cir. 2014)). "Fundamental differences between the references are central to th[e] motivation to combine inquiry." Adidas AG, 751 F.3d at 1359.

A skilled artisan's motivation to make a particular combination includes "whether he would select particular references in order to combine their elements." WBIP, LLC v. Kohler Co., 829 F.3d 1317, 1337 (Fed. Cir. 2016). "The inventor's own path itself never leads to a conclusion of obviousness. . . . What matters is the path that [a POSA] would have followed, as evidenced by the pertinent prior art." Otsuka Pharm. Co., Ltd. v. Sandoz, Inc., 678 F.3d 1280, 1296 (Fed. Cir. 2012).

"A prima facie case of obviousness typically exists when the ranges of a claimed composition overlap the ranges disclosed in the prior art." In re Peterson, 315 F.3d 1325, 1329 (Fed. Cir. 2003).

An overlap provides sufficient motivation to optimize the ranges. Id. at 1330 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of . . . ranges is the optimum combination.").

Broad ranges disclosed in prior art may preclude a finding of obviousness. See Genetics Inst., LLC v. Novartis Vaccines and Diagnostics, Inc., 655 F.3d 1291, 1306-07 (Fed. Cir. 2011) ("[T]he facts here present a case where the 'disclosed range is so broad as to encompass a very large[6] number of possible distinct compositions' thus 'requir[ing] nonobvious invention,' not a case, as in Peterson, where prior art 'ranges that are not especially broad invite routine experimentation to discover optimum values.").

Here, the parties do not dispute that a POSA would have been motivated to adapt Symbicort® from a DPI to a PMDI (Trial Trans. 101:10-12, 367:1-5, 842:1-9). The preference for pMDIs in the American market, coupled with the shift away from CFC propellants

[6] The patent at issue contained "68,000 truncated variants of a protein made up of 2,332 amino acids, and the allegedly interfering inventions differ[ed] in terms of the size of the permitted amino acid deletions, the location of those deletions, and the degree of allowable amino acid substitutions." Id.

following the Montreal Protocol, would have motivated a POSA to try to create a pMDI with an ICS and LABA. Id. at 101:10-102:2, 451:4-13, 360:2-7, 842:15-23. But given the dearth of prior art that taught towards a formulation with all of the claimed components of the claims at issue, it is unclear what would have prompted (or even enabled) a POSA at the priority date to select and combine all the elements of the claimed invention.

First, a POSA would have had to select both budesonide and formoterol as the active ingredients in the claimed formulation. Mylan argues that these were the active ingredients in the Symbicort® DPI already on the market. As established at trial, however, the formulation of a dry powder inhaler differs significantly from a pMDI. Therefore, even if a POSA had been motivated to use both budesonide and formoterol, a POSA's work would have just begun. Indeed, a POSA would have confronted additional choices concerning the concentrations of these medicaments in the formulation, whether to pursue a solution or a suspension, which grades of excipient and/or valve lubricant to use and in what concentrations, and which propellant or propellants to use. All of these choices, and the unpredictable ways each adjustment could impact the overall formulation, created an

insurmountable hurdle for a POSA.[7]

Second, to adapt the Symbicort® DPI to a pMDI, a POSA would have had to choose whether to pursue a solution or suspension formulation. A suspension formula most resembles a DPI because the drug particles remain in a solid state rather than dissolving into a smaller form and size, as they would in a solution. See, e.g., Trial Trans. 110:12-14, 141:1-8, 142:9-19, 143:18-147:23.

One of the "most important goals" of a formulator POSA would be to guarantee dose uniformity through the life of the device. Id. at 140:7-23, 611:23-25. Critically, particles from a DPI, designed to be used in a device that operates differently and to be co-blended with DPI-specific excipients, cannot be transferred wholesale to a pMDI propellant-based system. Id. at 622:6-25. Thus, the prior art did not teach using DPI particles in pMDIs, but instructed that the effective dose, based on particle size as emitted by the device, should match an existing CFC product (Dkt. No. 417 at 26). See also JTX 2353.0007, JTX 2392.0005, PTX 650.0006, Trial Trans. at 621:24-623:17. Keeping the same particle size used in the Symbicort® DPI therefore would likely not have

[7] See Attachment 1, "Choices Faced by the POSA", PDX-1.036.

been a choice available to a POSA using the prior art known at the priority date.

Next, a POSA would have had to know to use HFA 227 exclusively, rather than a blend of HFA 227 and HFA 134a, or just HFA 134a. Yet, as of the priority date, every FDA-approved HFA pMDI product used HFA 134a, not HFA 227 (JTX 2353.0013; Trial Trans. at 255:16-18, 653:14-16). Further, the density of budesonide and formoterol would cause these medicaments to sediment in HFA 134a but cream in HFA 227 (Dkt. No. 417 at 28). Formulations that cream, or float to the top of the liquid suspension, "can adhere substantially at the gas-liquid interface, preventing dose uniformity." Id. at 29; Trial Trans. at 657:16-658:19.

Critically, Controls 3 and 9 in the Rogueda prior art identified this issue. Unlike Rogueda's formulations using HFA 134a, the budesonide and formoterol formulations using HFA 227, PVP K25, and PEG-1000 adhered to the gas-liquid interface (JTX 2374.0028; Trial Trans. at 656:6-659:18). Therefore, if a POSA's primary concern was to duplicate the effective, proven, and consistent dosing in the Symbicort® DPI, the prior art at priority suggested that using HFA 227 likely would have been a fatal choice.

Finally, to arrive at the claimed formulation, a POSA would

have to use PVP K25 and PEG-1000 in specific concentrations. Although one of the prior art references at the time, Mistry, used six PVP grades within its most preferred ranges (17 PF, K29/32, K90, K120, C15, and C30), it did not use K25 (JTX 2381.0003, pp. 12-13; Trial Trans. at 311:12-312:5, 740:6-19). Thus, the long list of PEG grades and concentrations in Mistry would not have motivated a POSA to select PEG-1000 in a concentration of 0.3% w/w (JTX 2381.0015, Trial Trans. at 314:6-8, 732:5-6).

Given the "design space" in which a POSA found himself, Mylan argues a POSA would have undertaken "routine experimentation" and been guided by multiple references and his own knowledge that fewer than ten pharmaceutical grades of PVP and PEG, respectively, were commercially available at the priority date (including PVP K25 and PEG-1000) (Dkt. No. 418 at 18). It also contends that, from experience, a POSA would have understood that multiple grades would be screened at the same time during optimization. Id.

But this argument discounts the fact that Mistry disclosed twelve excipient polymers, with six different grades being "most preferred," and eleven lubricants—all of which would have required experimentation to determine the properties of each potential formulation. See Trial Trans. at 194:12-198:8. Moreover, a POSA

would have had to engage in extensive experimentation to arrive at the concentrations used in the patents-in-suit. See id. at 737:8-747:12 (Dr. Young opining that, without hindsight, and based on Mistry, a POSA would never have used PVP and PEG in the concentrations at issue here).

AstraZeneca argues that, had a POSA relied on Mistry's disclosures alone, the sheer number of potential formulations would have exceeded 2,560,000. See "Mistry's Disclosures Lead to a Very Large Number of Formulations," Attachment B. And, had a POSA considered other prior art references at the priority date, the number of possible combinations would have been even higher. Compare PDX-2.097, Attachment C, with id. Testing these formulations to determine whether or not the combination was viable would have taken an "eternity." Trial Trans: 746:22-747:12.

Mylan's argument amounts to simply experimenting in the "design space," and does not consider how different amounts of various ingredients could impact each other. See Allergan, Inc. v. Sandoz, Inc., 796 F.3d 1293, 1305 (Fed. Cir. 2015) ("[T]he record shows that the claimed amounts of the two different ingredients could and did materially and unpredictably alter the property of the claimed formulation."). Here, the number of possible

combinations disclosed by Mistry alone is in the millions. Therefore, at the priority date a POSA would not have been motivated to select the specific formulation claimed by the patents-in-suit.

2. Teaching Away

AstraZeneca argues that Rogueda's controls teach away from selecting formulations with budesonide, formoterol, HFA 227, PVP K25, and PEG-1000 because the combinations closest to the claimed formulation were unsuitable and left medication residue at the gas-liquid exchange barrier.

> "[W]here there is a range disclosed in the prior art, and the claimed invention falls within that range, a relevant inquiry is whether there would have been a motivation to select the claimed composition from the prior art ranges. In those circumstances, the burden of production falls upon th patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations."

Id. at 1304-05. A reference does not teach away if it "merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into the claimed invention." Meiresonne v. Google, Inc., 849 F.3d 1379, 1382 (Fed Cir. 2017). "A reference teaches

away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken in the claim." Id. "A reference that properly teaches away can preclude a determination that the reference renders a claim obvious." In re Moutett, 686 F.3d 1322, 1333 (Fed. Cir. 2012); see also Winner Intern. Royalty Corp. v. Wang, 202 F.3d 1340, 1349-50 (Fed. Cir. 2000).

Rogueda performed tests to compare his invention containing polar fluorinated molecules to several "control" formulations. Control 3 and Control 9 are relevant to the patents-in-suit because Control 3 contained formoterol, 0.001% w/w PVP K25, 0.1% w/w PEG-1000 in a density-matched blend of HFA 227 and HFA 134a, and Control 9 contained budesonide, 0.001% w/w PVP K25 and 0.3% w/w PEG-1000 in HFA 227. The claimed formulation at issue in this case contains budesonide, formoterol, 0.001% w/w PVP K25, 0.3% w/w PEG-1000, and HFA 227.

According to Mylan, Rogueda established that this formulation could be successfully created. The expert testimony at trial, however, established that formulations with budesonide or formoterol and PVP K25 and PEG-1000 adhered to the test cans at the

gas-liquid interface and had particle aggregation (JTX 2374 at pp. 27-28, 30-32; Trial Trans. at 680:1-686:21, 690:5-696:6). Based on this, AstraZeneca contends that a POSA would have expected that budesonide and formoterol formulations with PVP K25 and PEG-1000 would be unstable (Dkt. No. 417 at 13).

The experts at trial all agreed that dose uniformity and consistent dosing would be priorities for a POSA (Trial Trans. 262:13-268:15, 389:2-11, 601:13-25, 831:3-9). Therefore, the bare data in Rogueda, which was not even the focus of the testing at issue, does not support Mylan's argument that this prior art would have made the claimed invention obvious. It may be true that Rogueda did not necessarily disparage the formulations in Controls 3 and 9, but the data cut against the very goal a POSA would have been trying to achieve—a stable product with a consistent dose. Therefore, because a POSA would have been discouraged from incorporating the formulations in Controls 3 and 9, Rogueda teaches away and does not render the claims obvious.

3. Obvious to Select or Combine

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the

known options within his or her technical grasp." KSR, 550 U.S. at 421. "If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." Id.

Here, based on the prior art available at the priority date, there was no finite number of identified, predictable solutions. Rather, the prior art disclosed multiple grades of different excipients, different propellants, and various LABAs and inhaled corticosteroids that could be used. Therefore, without "clues pointing to the most promising combinations, an artisan could have spent years experimenting without success." Leo Pharm. Products, Ltd. v. Rea, 726 F.3d 1346, 1357 (Fed. Cir. 2013); Trial Trans. at 746:22-747:12. Consequently, even if the Court were to find Dr. Pritchard's "design space" argument persuasive, his proposed routine optimization would not have resulted in the claimed invention within a reasonable period of time. It therefore would not have been obvious to try based on the prior art available to a POSA at the priority date.

4. Reasonable Expectation of Success

The experts all agree that a POSA would have required a formulation having dose uniformity (Trial Trans. 262:13-268:15,

389:2-11, 601:13-25, 831:3-9). The expectation of success is assessed in view of this goal. See Institut Pasteur & Universite Pierre et Marie Curie v. Focarino, 738 F.3d 1337, 1346-47 (Fed. Cir. 2013). "[T]here can be little better evidence negating an expectation of success than actual reports of failure." See In re Cyclobenzaprine, 676 F.3d at 1081.

As the Court has discussed, the prior art taught that budesonide formulations with PVP K25 and PEG-1000 undesirably adhered to the device at the liquid-gas interface. Therefore, a POSA would not have had a reasonable expectation of success in creating a stable budesonide pMDI using HFA 227, PVP K25, and PEG-1000, much less when these ingredients were combined with formoterol.

5. Unexpected Properties

Because Mylan has failed to carry its burden of proving a motivation to select and combine the elements of the claims, Otsuka, 678 F.3d at 1296, the Court need not reach the issue of unexpected properties. Even so, Mylan's arguments on this issue are unavailing. Unexpected properties are present where "the claimed invention exhibits some superior property or advantage" that a POSA "would have found surprising or unexpected." Procter & Gamble v.

Teva Pharm., 566 F.3d 989, 994 (Fed. Cir. 2009). Evidence of unexpected properties need only be "reasonably commensurate with the scope of the claims." In re Huai-Hung Kao, 639 F.3d 1057, 1068 (Fed. Cir. 2011).

Here, AstraZeneca's succeeded in its patent prosecution when it demonstrated the superior stability of its formulation with 0.001% w/w PVP K25. Mylan stresses that all tested formulations of Symbicort® with varying concentrations of PVP K25 had the same stability over the first fifteen seconds after shaking. But as Dr. Young opined this would not render the rest of the data irrelevant to a POSA (Trial Trans. at 752:3-15, 758:16-759:22). Indeed, a POSA would understand the formulation's stability after fifteen seconds to be an unexpected superior property when compared to Rogueda Control 9, which, as a whole, teaches away from the claims. Id. at 755:21-758:1. Accordingly, because an embodiment within the scope of the claims had unexpected properties, the claims are valid and not obvious.

IV. CONCLUSION

For the reasons discussed, the Court determines that Mylan has failed to carry its burden of proving obviousness by clear and convincing evidence.

It is so **ORDERED.**

The Clerk is directed to enter separate judgment orders in favor of Plaintiffs, AstraZeneca AB and AstraZeneca Pharmaceuticals LP, in Civil Action Nos. 1:18cv193 and 1:19cv203, and to transmit copies of these orders to counsel of record.

DATED: March 2, 2021

/s/ Irene M. Keeley
IRENE M. KEELEY
UNITED STATES DISTRICT JUDGE